

Serial No. 09/232,290

Listing of claims

Claims 1-41 (canceled)

1 ~~42~~ (New) A nucleic acid sequence encoding a modified single chain Fv molecule, wherein said single chain Fv molecule comprises a heavy chain variable domain and a light chain variable domain that interact to form an antigen binding site, wherein said heavy chain variable domain comprises an intra-heavy chain inter-domain interface region and said light chain variable domain comprises an intra-light chain inter-domain interface region

and wherein at least one amino acid in an intrachain inter-domain interface region is modified so as to decrease the hydrophobicity in said intra-chain inter-domain interface region.

2 ~~43~~ (New) A nucleic acid sequence encoding a modified polypeptide comprising a heavy chain variable domain, wherein said heavy chain variable domain comprises an intra-heavy chain inter-domain interface region,

and wherein at least one amino acid in said intra-heavy chain inter-domain interface region is modified so as to decrease the hydrophobicity in said region.

3 ~~44~~ (New) The nucleic acid sequence according to claim ~~43~~², wherein said intra-heavy chain inter-domain interface comprises residues 9, 10, 11, 13, 14, 41, 42, 43, 84, 87, 89, 105, 108, 110, 112, 113 of said heavy chain variable domain.

4 ~~45~~ (New) A nucleic acid sequence encoding a modified polypeptide comprising a light chain variable domain, wherein said light chain variable domain comprises an intra-light chain inter-domain interface region,

and wherein at least one amino acid in said intra-light chain inter-domain interface region is modified so as to decrease the hydrophobicity in said region.

5 ~~46~~ (New) The nucleic acid sequence according to claim ~~45~~⁴, wherein said inter-domain interface comprises residues 9, 10, 12, 15, 39, 40, 41, 80, 81, 83, 103, 105, 106, 106A, 107, 108 of said light chain variable domain.

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⁶ ~~47~~. (New) The nucleic acid sequence according to claim ¹ ~~42~~ in which said modification comprises insertion of one or more hydrophilic amino acids or deletion of one or more hydrophobic amino acids.

⁷ ~~48~~. (New) The nucleic acid sequence according to claim ¹ ~~42~~ in which said modification comprises any two or more of:

- a) a substitution of one or more amino acids with amino acids which are more hydrophilic than the one or more amino acids being substituted for;
- b) an insertion of one or more hydrophilic amino acids; and
- c) a deletion of one or more hydrophobic amino acids.

⁸ ~~49~~. (New) The nucleic acid sequence according to claim ⁶ ~~47~~ or ⁷ ~~48~~ in which said substituted or inserted amino acid is selected from the group consisting of Asn, Asp, Arg, Gln, Glu, Gly, His, Lys, Ser, and Thr.

⁹ ~~50~~. (New). The nucleic acid sequence according to claim ^{2 3 5} ~~46~~, ~~47~~, or ~~48~~, further comprising a contiguous sequence which encodes one or more additional moieties.

⁹ ~~51~~. (New) The nucleic acid sequence according to claim ⁹ ~~50~~ in which at least one of said additional moieties is a toxin, a cytokine, or a reporter enzyme.

¹⁰ ~~52~~. (New) The nucleic acid sequence according to claim ¹⁰ ~~51~~ in which at least one of said additional moieties is at least part of a surface protein of an organism.

¹¹ ~~53~~. (New) The nucleic acid sequence according to claim ¹¹ ~~52~~ in which said organism is a filamentous bacteriophage.

¹² ~~54~~. (New) The nucleic acid sequence according to claim ¹² ~~53~~ in which said surface protein is the geneIII protein.

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14/5. (New) The nucleic acid sequence according to claim 9/10 in which at least one of said additional moieties is capable of binding a metal ion.

15/56. (New) The nucleic acid sequence according to claim 14/56 in which at least one of said additional moieties comprises at least five histidines.

16/7. (New) The nucleic acid sequence according to claim 9/50 in which said additional moiety is a labeling tag peptide.

17/58. (New) The nucleic acid sequence according to claim 16/57 in which said labeling tag peptide is c-myc or FLAG.

18/59. (New) The nucleic acid sequence according to claim 9/60 in which said additional moiety comprises a peptide comprising an association domain..

19/60. (New) The nucleic acid sequence according to claim 18/59 in which said association domain comprises a leucine zipper or a helix-turn-helix motif.

3/20/61. (New) A vector comprising a nucleic acid sequence according to claim 1/2, 4/43, or

21/62. (New) A host cell comprising a vector according to claim 20/61.

22/63. (New) The nucleic acid sequence according to claim 1/62, wherein at least one amino acid in said intra-heavy chain inter-domain interface and at least one amino acid in said intra-light chain inter-domain interface is modified.